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RELATIONSHIP BETWEEN SERUM BIOMARKERS OF TYPE II COLLAGEN (C2C; C1,2C AND CP II) AND RADIOLOGICAL PATTERNS IN PATIENTS WITH HIP OSTEOARTHRITIS

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Background: Cartilage destruction in osteoarthritis (OA) involves excessive degradation and increased synthesis of cartilage matrix macromolecules including type II collagen and proteoglycans. Cartilage biomarkers exist for the measurement of changes in cartilage matrix turnover.
Aim: To determine whether there is a relationship between serum levels of type II collagen degradation and synthesis biomarkers (C2C, C1,2C and CP II) and radiological data in patients with hip OA and generalized OA.
Patients and methods: 56 patients (mean age/SD: 62/11; BMI/SD: 27/11) with symptomatic hip OA (Lequesne index/SD: 8.3/4.). Minimum joint space width (Min JSW) was obtained by computer measurement. The following serum markers were studied using commercial kits from Ibex Diagnostics (Montreal, QC): type II collagen synthesis C-propeptide (CPII), cleavage by collagenase of type II (C2C) and types I and II (C1, 2C) collagens. The other studied variables were: age, sex, BMI, hip OA bilaterality, and the number of involved joints. Patients with OA affecting more than 3 different joints were classified has having generalized OA (GOA).
Statistics: Multivariate analysis
Results Unilateral hip OA without any other joint involvement was observed in 17 patients.Twenty two patients had bilateral hip OA and 24 GOA. MinJSW was 2.23±1.25 mm.
There was a correlation between min JSW and C2C in patients with unilateral hip OA (R=0.50, p= 0.02).
CPII levels were significantly lower in patients with GOA (99.9±50.3ng/mL versus 141.9±81.2ng/mL, p=0.04, OR= 0.18 for CPII >120 ng/mL, [CI-95% 0.05-0.6], p<0.005).
Conclusion: Differences in the pathogenesis of hip OA can be distinguished by systemic measurement of certain cartilage biomarkers. Generalized OA may be due to a deficiency in a reparative process involving type II collagen. The significant correlation between C2C and JSW in unilateral hip OA suggests that this marker is of value in assessing cartilage degradation in patients with involvement of a single hip joint.

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ASSOCIATION BETWEEN URINARY CONCENTRATIONS OF TYPE II COLLAGEN NEOEPITOPE (uTIINE) AND JOINT SPACE NARROWING (JSN) IN SUBJECTS WITH KNEE OSTEOARTHRITIS (OA)

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Purpose: Matrix metalloproteinases cleave the Type II collagen helix into 3/4- and 1/4-length fragments. Urinary levels of neoepitopes on the larger fragment (uTIINE)have been shown to differentiate symptomatic OA from asymptomatic disease. This pilot study asked whether (a) baseline uTIINE levels predict radiographic and symptomatic progression of knee OA and (b) serial values reflect concurrent JSN.
Methods: Subjects were 120 women with unilateral knee OA who completed a 30-mo RCT of structure-modification by doxycycline (doxy). Sixty were x-ray progressors (mean JSN ± SD = 0.97 ± 0.75 mm); 60 were non-progressors (-0.03 ± 0.17 mm).
Each group contained 30 subjects who exhibited clinically significant increases in knee pain over 30 mos and 30 who did not. Urine samples were collected every 6 mos for analysis of uTIINE with an antibody capture assay that measured the levels of a 45-mer peptide resulting from collagenase cleavage of Type II collagen. uTIINE values were normalized for urinary creatinine (Cr).
Results: Results of logistic regression analyses to predict JSN and knee pain are shown in Table 1. In the placebo group, uTIINE was unrelated to JSN or knee pain. However, in the doxy group, a 1-SD increment in baseline uTIINE (68 ng/mM Cr) was associated with a 2-fold increase in odds of progression of JSN (OR 2.04, *P*=0.058).

Table 1. Prediction of JSN and Knee Pain

Outcome	Placebo Group (N = 69) uTIINE SD = 64 ng/mM Cr		Doxy Group (N = 51) uTIINE SD = 68 ng/mM Cr	
	Odds Ratio*	95% CI	Odds Ratio*	95% CI
JSN	0.74	0.44 - 1.23	2.04	0.98 - 4.28
Knee Pain	0.71	0.41 - 1.23	0.80	0.43 - 1.50

*Change in odds of progression of JSN per 1-SD increase in the baseline uTIINE concentration, adjusted for baseline JSW and baseline VAS score for 50-ft Walk Pain. Odds ratios for prediction of knee pain were adjusted also for baseline BMI.

In an analysis of JSN over discrete time intervals, mixed models showed that both the mean and maximum of the intercurrent uTIINE values were associated with JSN (Table 2).

Table 2. Concurrent Association Between uTIINE and JSN

Intercurrent uTIINE	0-16 Month Interval		16-30 Month Interval	
	SD of uTIINE	Parameter Estimate*	SD of uTIINE	Parameter Estimate*
Mean	69	0.10‡	66	0.17‡§
Maximum	108	0.14‡	98	0.10†

*Parameter Estimate = change in JSN, in mm, associated with a 1-SD increase in mean or maximum uTIINE concentration (ng/mM Cr) after adjustment for age, knee and JSW at the start of the interval. †P<0.05; ‡P<0.01; § A significant uTIINE by Treatment Group interaction was detected (P<0.05). The data shown represent the association between mean uTIINE levels and JSN in the placebo group only.

Conclusion: uTIINE was not a consistent predictor of JSN or knee pain in subjects with knee OA. However, serial uTIINE values reflected concurrent JSN.
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ARE INFLAMMATORY CYTOKINES PREDICTORS OF SYMPTOM RESPONSE TO WEIGHT LOSS IN OVERWEIGHT AND OBESE PERSONS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS (OA)?

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Study Aims: To evaluate whether baseline levels of interleukin (IL)-1, IL-6 or tumor necrosis factor (TNF)-α are associated with